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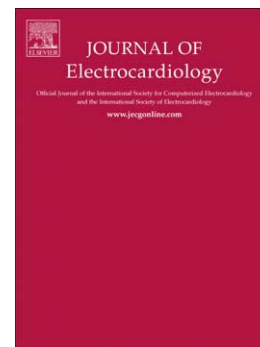
## Accepted Manuscript

Appropriateness of antero-septal myocardial infarction nomenclature evaluated by late gadolinium enhancement cardiovascular magnetic resonance imaging

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**Appropriateness of anteroseptal myocardial infarction nomenclature evaluated by late gadolinium enhancement cardiovascular magnetic resonance imaging**

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**Running head:** Appropriateness of anteroseptal MI ECG nomenclature

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## ABSTRACT

### *Background*

In traditional literature, it appears that “anteroseptal” MIs with Q waves in V1-V3 involve basal anteroseptal segments although studies have questioned this belief.

### *Methods*

We studied patients with first acute anterior Q-wave ( $>30\text{ms}$ ) MI. All underwent late gadolinium enhancement (LGE) cardiac magnetic resonance imaging (MRI).

### *Results*

Those with Q waves in V1-V2 ( $n=7$ ) evidenced LGE  $>50\%$  in 0%, 43%, 43%, 57%, and 29% of the basal anteroseptal, mid anteroseptal, apical anterior, apical septal segments, and apex, respectively. Patients with Q waves in V1-V3 ( $n=14$ ), evidenced involvement was 14%, 43%, 43%, 50%, and 7% of the same respective segments. In those with extensive anterior Q waves ( $n=7$ ), involvement was 0%, 71%, 57%, 86%, and 86%.

### *Conclusions*

Q-wave MI in V1-V2/V3 primarily involves mid- and apical anterior and anteroseptal segments rather than basal segments. Data do not support existence of isolated basal anteroseptal or septal infarction. “Anteroapical infarction” is a more appropriate term than “anteroseptal infarction.”

**Key words:** Electrocardiography, myocardial infarction, magnetic resonance imaging, Q waves, anterior wall myocardial infarction, anteroseptal myocardial infarction

## INTRODUCTION

Isolated Q waves in leads V1-V3 of the electrocardiogram (ECG), with or without extension to V4, have traditionally denoted “anteroseptal” myocardial infarction (MI), while isolated Q waves found in leads V1-V2 have been termed “septal” MI. The origin of these definitions stems from histopathological studies carried out several decades ago.<sup>1,2</sup> Given the selection bias inherent in such works, the external validity of these findings has reasonably been brought into question.

More recent studies have attempted to address the controversy through correlations of the ECGs with angiography or advanced cardiac imaging modalities. Shalev et al. concluded that the traditional definition of isolated anteroseptal MI is not supported by angiographic and echocardiographic data and that the actual infarcted area is in fact more anteroapical with minimal septal involvement.<sup>3</sup> Bogaty et al. reported somewhat similar findings, suggesting that the area of infarct is apical but still involves the septum in a majority of patients.<sup>4</sup> Unfortunately, both studies were limited by the inability of echocardiography to distinguish between stunned and infarcted myocardium.

In the context of MI, late gadolinium enhancement cardiovascular magnetic resonance imaging (LGE MRI) is especially useful for noninvasive assessment of infarct tissue volume and extent of transmural involvement with high spatial resolution.<sup>5-7</sup> In a set of 19 patients with acute MI and new Q waves in leads V1 to V2-V4, Selvanayagam et al. used LGE MRI to suggest predominantly apical infarction with some involvement of the mid-ventricular anteroseptum.<sup>6</sup> However, this study was marked by nebulous inclusion criteria, as patients with more extensive anterior Q waves were grouped together with those with limited “anteroseptal” Q waves in the analysis.

We aimed to assess the extent and location of pre-discharge LGE in patients with traditional “anteroseptal” MI (Q waves in V1-V3) and to compare this to the pattern seen in patients with more extensive distribution of Q waves in the precordial leads. We hypothesize that the ECG diagnosis traditionally termed “anteroseptal” MI, actually denotes an area of apical infarction, rather than basal anteroseptal MI, as is often thought and taught.

## METHODS

We conducted a multicenter retrospective cohort analysis of patients undergoing LGE cardiac MRI at sites in the United States and Europe. We incorporated data from the MITOCARE study, patients from the Houston Methodist Hospital (Houston, Texas, USA) and the Texas Heart Institute, Baylor St. Luke’s Medical Center (Houston, Texas, USA). Details of the MITOCARE study have been previously released.<sup>8,9</sup>

Inclusion criteria were admission to the hospital with a first acute anterior MI and pre-discharge ECG demonstrating Q or QS waves (>30 ms) in leads V1 up to V6. ECGs were reviewed by the ECG laboratory, which was blinded to the results of LGE cardiac MRI.

Eligible patients had undergone LGE cardiac MRI after this index cardiac event on whole-body magnetic resonance scanners with cardiac applications used for standard clinical cardiac magnetic resonance (CMR).<sup>8,10</sup>

The following parameters were collected by a separate observer, examining CMR short-axis images during end-diastole and end-systole: left ventricular mass (g), stroke volume (in mL), left ventricular ejection fraction (LVEF) (graded by percentage), and the transmural extent of LGE (graded by percentage). In order to uniformly describe the distribution of LGE, we have used the American Heart Association (AHA) 17-segment model for description of myocardial segments.<sup>11</sup> LGE was quantified using planimetry. To compare categorical variables, the  $\chi^2$  test or Fisher's exact test were carried out. One-way analysis of variance (ANOVA) was used to compare continuous variables. A *p*-value <0.05 was considered statistically significant for the purposes of this study. Values herein are described as median or mean  $\pm$  standard deviation (SD) as appropriate. Frequencies and percentages have been used to describe categorical variables. The study was approved by the institutional review board at Baylor College of Medicine in Houston, Texas.

## RESULTS

A total of 28 patients qualified for inclusion in the study. Thirteen patients were recruited from the MITOCARE study, ten from the cardiac MRI database of the Houston Methodist Hospital and five from the cardiac MRI database of the Texas Heart Institute at Baylor St. Luke's Medical Center. The mean age of the patients was  $61 \pm 18$  years. Twenty-six patients (93%) were male. Eight (28%) had diabetes mellitus, 15 (54%) had hyperlipidemia, and 13 (46%) had hypertension. Nineteen patients (68%) were current or



former users of tobacco products. (Table 1). Patients in the MITOCARE trial underwent primary percutaneous coronary interventions according to the study protocol.<sup>8</sup>

Seven patients had Q waves in leads V1-V2, fourteen had Q waves in leads V1-V3, and seven patients had Q waves extending up to lead V6. In this last group, the distribution of Q waves was as follows: V1-V4: two patients; V1-V6: one patient; V2-V6: two patients; V3-4: one patient; V3-V6: one patient.

The median time from index MI to the inclusion ECG was three days for all patients; the median time from the index MI to LGE cardiac MRI was four days. Mean LVEF across the entire cohort was  $42.7 \pm 17\%$ , and mean LV myocardial mass was  $144 \pm 45$  g (Table 1). Both LVEF and LV myocardial mass were not statistically different among the three groups.

There was a statistically significant increase in the mean number of affected myocardial segments as well as a larger infarct size with more extensive Q wave distributions (Table 1).

Tables 2 and 3 depict the extent of LGE across the 17 myocardial segments in the three different Q wave infarct territories.

In patients with Q waves only in leads V1-V2 ( $n = 7$ ),  $>25\%$  LGE was seen in zero (0%), three (43%), four (57%), four (57%), and three (43%) patients in the basal anteroseptal (segment 2), mid anteroseptal (segment 8), apical anterior (segment 13), apical septal (segment 14) and apex (segment 17), respectively (Table 2). Within this same group,  $>50\%$  LGE was seen in zero (0%), three (43%), three (43%), four (57%), and two (29%) patients at the same segments, respectively (Table 3).

In those with Q waves in leads V1-V3 ( $n = 14$ ), LGE  $>25\%$  was seen in three (21%), nine (64%), seven (50%), nine (64%), and ten (71%) patients in the basal anteroseptal, mid anteroseptal, apical anterior, apical septal segments, and apex, respectively (Table 2). In the same group, LGE  $>50\%$  was seen in two (14%), six (43%), six (43%), seven (50%), and seven (50%) patients at the same respective segments (Table 3).

In the group of patients with anterior Q waves extending up to V6 ( $n = 7$ ), one (14%), six (86%), six (86%), six (86%), and seven (100%) patients were found to have LGE  $>25\%$  in at the basal anteroseptal, mid anteroseptal, apical anterior, apical septal segments, and apex, respectively (Table 2). A similar pattern was observed when comparing the distribution of segments with  $>50\%$  LGE involvement: zero (0%), five (71%), four (57%), six (86%), and six (86%) patients, respectively (Table 3).

Thus, a trend toward greater involvement of the apical segments was noted with more extensive anterior Q waves. However, this was not found to be statistically significant (Tables 2 and 3).

## DISCUSSION

The ECG has been the bedrock of MI diagnosis for many years. Much of the traditional ECG pedagogy for MI is somewhat skewed given the inherent bias of histopathological studies, on which these presumptions were initially made. As CMR techniques have advanced, the use of LGE cardiac MRI affords the unique opportunity to accurately visualize areas of myocardial infarction with the highest sensitivity of available imaging techniques.<sup>7</sup>

Using LGE MRI, Selvanayagam et al. showed predominantly apical infarction with some involvement of the mid-ventricular anteroseptum in 19 patients with acute MI and new Q waves in the precordial leads including leads V1-V4.<sup>6</sup> A major weakness of this study was that only eight study patients actually exhibited Q waves in the “anteroseptal” leads V1-V3, while the remainder (n=11), showed more extensive Q waves up to V5 and V6. This latter group was not excluded from analysis or compared to the “anteroseptal” MI group, although it did not technically fulfill “anteroseptal” MI criteria. Our study greatly improves upon this work as we have tightly delineated Q-wave MIs based upon several anteroseptal ECG patterns (Q waves in “septal” leads V1-V2 and leads V1-V3), and patients with extensive anterior MI have been analyzed separately.

We used the traditional definitions of “septal” and “anteroseptal” infarction with Q waves in leads V1-2 and leads V1-V3/V4, respectively.<sup>12</sup> We were able to compare the extent of LGE in patients presenting with so-called “anteroseptal” or “septal” MIs to those presenting with more extensive Q waves in the anterior leads, from lead V1 up to V6. Basal septal involvement was relatively rare in all three groups of patients. An ECG of a study patient demonstrating this classical definition of anteroseptal infarction is shown in Figure 1, with the corresponding cardiac MRI LGE images.

An examination of the distribution of LGE across the myocardial segments (Tables 1 to 3) reveals that more extensive anterior Q waves were associated with greater extent of LGE and a trend toward more involvement of the apical segments. However, apical segment involvement was most prominent even in those with so-called “anteroseptal” and “septal” MIs. Most interestingly, none of the patients with Q waves in “septal” leads

V1-V2 showed LGE in the basal anteroseptal segment, while the apical anterior and septal segments were frequently involved.

The mid anteroseptal segment was still affected in those with Q waves extending to V2 and V3 although it seems that the apex, apical anterior, and apical segments are still more frequently affected. Most significantly, no patient evidenced lone septal or lone basal anteroseptal LGE, which runs quite contrary to the traditional terminology. In fact, a prominent online course on ECG interpretation produced by the American Heart Association teaches that anteroseptal infarction involves only the basal anteroseptal segments.<sup>13</sup> Recent investigations have suggested that ECG patterns with Q waves in traditionally labelled anteroseptal territories may be more granularly detailed into such categories as “septal,” “apical anteroseptal,” “extensive anterior,” and “limited anterior.”<sup>14,15</sup> It seems that although the anteroseptal segments are still affected, the primary segments of involvement are apical. As such, we propose that the term “anteroapical” be used as a more accurate descriptor for the ECG entity currently known as “anteroseptal” myocardial infarction, corroborating the suggestion by Shalev et al. and Bogaty et al.<sup>3,4</sup>

Thus, the traditional thought that Q waves in leads V1-V3 represent lack of electrical activity in the left ventricular segments underneath these electrodes is wrong. The electrical activation of the left ventricle begins at three points (the anterior paraseptal wall, the posterior paraseptal wall and the center of the left side of the septum). Septal activation begins from the left to the right side and from the apex to base. Thus, Q waves in leads V1-V3 may represent diminution of the initial activation vector from the apex to the base of the heart due to apical infarction.<sup>16</sup>

Although it may be convenient to name the anterior ECG leads based upon anatomic overlay of the heart, translating this nomenclature to MI territories is not entirely accurate. Though patients with Q waves in V1-V3 may evidence concurrent mid anteroseptal LGE, the basal anteroseptum is rarely involved, so “anteroseptal infarction” does not seem to be an accurate label.

#### *Future work and directions*

The relatively young field of cardiovascular MRI is fertile ground for disruption of the traditional definitions of myocardial infarction as well as many other entities that may be diagnosed with the 12 lead ECG. Although the ECG is crucial to diagnosis in cardiology, more investigations of traditional ECG terminology is needed, especially with respect to territorial description of MIs. Studies of larger groups of patients would be valuable. However, the expense and limited availability of cardiovascular MRI has been a barrier to wider spread use of this useful imaging modality, except at larger medical centers.

#### *Limitations*

Our study does have its own set of limitations. It should be noted that this patient cohort may not have captured silent MIs, which may represent an entire entity on their own. The retrospective nature of the study carries its own set of limitations as there may be unmeasured confounding factors interfering with analysis.

#### **Conclusions**

Acute MIs with Q waves in leads V1-V2 or V1-V3 primarily involve the mid- and apical anterior and anteroseptal segments rather than the basal segments. These data do not support the existence of isolated basal anteroseptal or septal infarction. The term “anteroapical infarction” is more appropriate than “anteroseptal infarction” for an ECG showing Q waves in V1-V3.

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### **Conflicts of Interest**

Einar Heiberg is founder of Medviso AB, developing cardiovascular image processing software. Marcus Carlsson is employed by Imacor AB. Håkan Arheden is founder of and employed by Imacor AB

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## TABLES AND FIGURES

**Table 1.** A description of myocardial segments affected left ventricular ejection fraction (LVEF), and myocardial mass for the different Q wave distributions. Values are reported as mean $\pm$ standard deviation (SD) when applicable. *P* values are the result of ANOVA comparing the sample means among the three groups.

ECG Q- wave distribution	V1-V2	V1-V3	>V3	<i>P</i> value	All groups
Number of patients	7	14	7	-	28
Age (years)	61.4 $\pm$ 14.0	67.4 $\pm$ 13.4	61.2 $\pm$ 13.6	0.517	60.8 $\pm$ 17.7
Male (%)	86	93	100	0.74	93
Caucasian (%)	57	93	100	0.07	86
Diabetes (%)	57	21	14	0.23	29
Hyperlipidemia (%)	71	64	14	0.07	54
Hypertension (%)	71	57	14	0.06	46
Tobacco use (%)	86	57	71	0.39	68
Myocardial segments with LGE	4.7 $\pm$ 3.6	8.6 $\pm$ 4.0	11.1 $\pm$ 2.1	0.006	7.9 $\pm$ 4.0
Myocardial scar (g)	10.4 $\pm$ 11.3	33.1 $\pm$ 23.2	44.4 $\pm$ 18.8	0.029	-
Myocardial mass (g)	139.4 $\pm$ 22.5	160.1 $\pm$ 42.7	144.8 $\pm$ 24.4	0.455	-
LVEF (%)	43.7 $\pm$ 28.1	44.2 $\pm$ 16.8	42.8 $\pm$ 8.8	0.99	42.7 $\pm$ 16.8

**Table 2.** Number of patients with >25% late gadolinium enhancement grouped by ECG

Q wave distribution. P values are computed by Fisher's exact test.

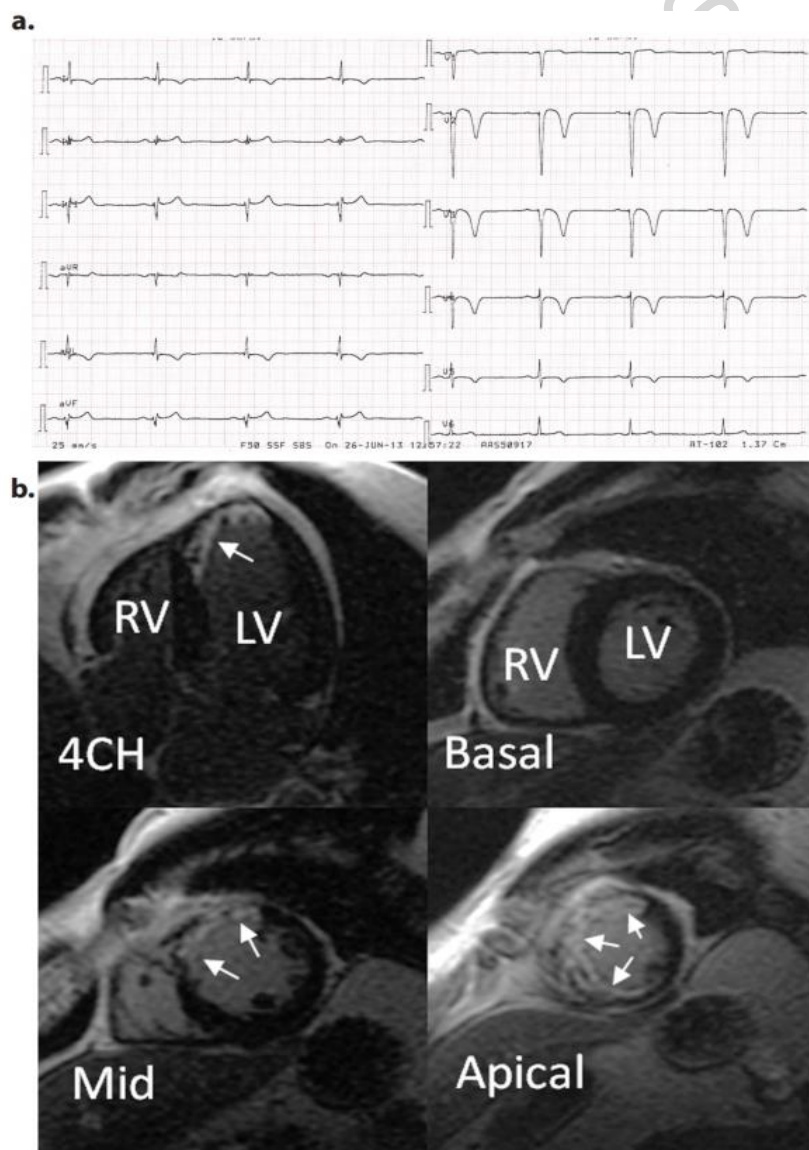
Segment number	Myocardial Segment	Q wave distribution			P value
		V1-V2, n (%)	V1-V3, n (%)	>V3, n (%)	
1	Basal anterior	2 (29%)	1 (7%)	0 (0%)	0.2
2	Basal anteroseptal	0 (0%)	3 (21%)	1 (14%)	0.66
3	Basal inferoseptal	0 (0%)	1 (7%)	0 (0%)	0.99
4	Basal inferior	0 (0%)	1 (7%)	0 (0%)	0.99
5	Basal inferolateral	0 (0%)	1 (7%)	0 (0%)	0.99
6	Basal anterolateral	0 (0%)	1 (7%)	0 (0%)	0.99
7	Mid anterior	4 (57%)	7 (50%)	4 (57%)	0.99
8	Mid anteroseptal	3 (43%)	9 (64%)	6 (86%)	0.24
9	Mid inferoseptal	0 (0%)	6 (43%)	1 (14%)	0.08
10	Mid inferior	0 (0%)	2 (14%)	0 (0%)	0.48
11	Mid inferolateral	0 (0%)	0 (0%)	0 (0%)	1
12	Mid anterolateral	0 (0%)	1 (7%)	1 (14%)	0.74
13	Apical anterior	4 (57%)	7 (50%)	6 (86%)	0.32
14	Apical septal	4 (57%)	9 (64%)	6 (86%)	0.59
15	Apical inferior	1 (14%)	6 (43%)	3 (43%)	0.41
16	Apical lateral	0 (0%)	2 (14%)	3 (43%)	0.08
17	Apex	3 (43%)	10 (71%)	7 (100%)	0.06

**Table 3.** Number of patients with >50% late gadolinium enhancement grouped by ECG

Q wave distribution. *P* values are computed by Fisher's exact test.

Segment number	Myocardial Segment	Q wave distribution			<i>P</i> value
		V1-V2, n (%)	V1-V3, n (%)	>V3, n (%)	
1	Basal anterior	2 (29%)	1 (7%)	0 (0%)	0.2
2	Basal anteroseptal	0 (0%)	2 (14%)	0 (0%)	0.48
3	Basal inferoseptal	0 (0%)	0 (0%)	0 (0%)	1.0
4	Basal inferior	0 (0%)	1 (7%)	0 (0%)	0.99
5	Basal inferolateral	0 (0%)	0 (0%)	0 (0%)	1.0
6	Basal anterolateral	0 (0%)	0 (0%)	0 (0%)	1.0
7	Mid anterior	3 (43%)	3 (21%)	4 (57%)	0.17
8	Mid anteroseptal	3 (43%)	6 (43%)	5 (71%)	0.44
9	Mid inferoseptal	0 (0%)	2 (14%)	0 (0%)	0.48
10	Mid inferior	0 (0%)	0 (0%)	0 (0%)	1.0
11	Mid inferolateral	0 (0%)	0 (0%)	0 (0%)	1.0
12	Mid anterolateral	0 (0%)	0 (0%)	1 (14%)	0.25
13	Apical anterior	3 (43%)	6 (43%)	4 (57%)	0.79
14	Apical septal	4 (57%)	7 (50%)	6 (86%)	0.32
15	Apical inferior	0 (0%)	5 (36%)	0 (0%)	0.05
16	Apical lateral	0 (0%)	1 (7%)	1 (14%)	0.74
17	Apex	2 (29%)	7 (50%)	6 (86%)	0.11

**Figure 1.** An ECG showing Q waves in leads V1-V3 and T wave inversion in I,aVL, V2-V5 (a). The corresponding cardiac MRI LGE images (bottom) in the 4-chamber view (4CH), basal, mid and apical short-axis view showing contrast enhancement (arrows) in the apex, apical and mid-ventricular septal and anterior segments indicating infarct in these left ventricular segments. There is no contrast enhancement and thus no infarct in the basal segments. LV = left ventricle; RV = right ventricle.



**Highlights**

- MI with Q V1 to V2 or V3 involves mid/apical anterior and anteroseptal segments.
- No data support the existence of isolated basal anteroseptal or septal infarction.
- “Anteroapical infarction” is a more appropriate term than “anteroseptal infarction”